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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,533	09/15/2005	Firelli Alonso-Caplen	AM100395	7874
25291	7590	11/13/2008	EXAMINER	
WYETH			HURT, SHARON L	
PATENT LAW GROUP			ART UNIT	PAPER NUMBER
5 GIRALDA FARMS				1648
MADISON, NJ 07940				
			MAIL DATE	DELIVERY MODE
			11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/549,533	ALONSO-CAPLEN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	SHARON HURT	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 June 2008.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 4-17 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-3 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ .  | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

### ***Response to Amendment***

The amendments to the claims filed June 27, 2008 have been acknowledged and entered.

Claim 1 is currently amended.

### ***Status of the Claims***

Claims 1-17 are pending. Claims 4-17 have been withdrawn from consideration. Claims 1-3 are under examination.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. in view of Firestone et al. is maintained.**

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (Journal of Virology, Apr. 1998, Vol. 72, No. 4, pages 2871-2880) in view of Firestone et al. (Virology, 1996, Vol. 225, pages 419-422, Article No. 0618, Short Communication).

The claimed invention is drawn to a method of identifying an attenuated respiratory syncytial virus (RSV) strain that produces high yields of RSV surface glycoprotein F when compared to parent strain A2. The method comprises: providing a eukaryotic cell culture, infecting the cell culture with a live, attenuated RSV; and determining the glycoprotein F concentration, wherein at least five-fold increase in glycoprotein F concentration is an indication

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that the attenuated strain produces high yields of RSV F and G glycoproteins compared with the parent A2 strain, wherein the RSV mutant strain is *cpts*-248/404, wherein the eukaryotic cells are VERO, MRC-5, FRhl, CEF or PER.C6 cell culture.

Johnson et al. (hereinafter Johnson) teaches the G glycoprotein has been implicated as an RSV antigen that promotes activation of the Th2 CD4+ T-lymphocyte and induces eosinophilic infiltrates in the lung following RSV challenge (page 2871, 1<sup>st</sup> column, 1<sup>st</sup> paragraph). Johnson teaches the large glycoprotein G serves as the attachment protein of RSV and is one of the major glycoproteins expressed in the membrane of the virus. The protein is expressed on the surface of the infected cell and secreted into the extracellular environment (page 2871, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph). Johnson teaches use of recombinant vaccinia virus expressing RSV G (vacG) to prime mice generated a TH2 CD4+ T lymphocyte response, while vaccination with fusion (F) protein-expressing virus (vacF) induced a Th1 CD4+ T-cell response (page 2871, 2<sup>nd</sup> column, 2<sup>nd</sup> paragraph). Johnson also teaches a method of purifying and measuring the G-specific antibody in secreted RSV G protein from RSV A2 strain (page 2872, 1<sup>st</sup> column, 3<sup>rd</sup> paragraph and page 2873, 1<sup>st</sup> column, 1<sup>st</sup> paragraph). Johnson teaches mice vaccinated with vvWT G were found to have more severe illness and weight loss following challenge than mice immunized with vacF (page 2873, 1<sup>st</sup> column, 3<sup>rd</sup> full paragraph). Johnson teaches a study of viral challenge following vaccination wherein the results indicate that G is less immunogenic than F (page 2873, 2<sup>nd</sup> column, 1<sup>st</sup> paragraph). Johnson does not teach an attenuated RSV, mutant strain *cpts*-248/404 or using VERO cells.

Firestone et al. (hereinafter Firestone) teaches a live attenuated RSV strain, *cpt*-248/404 mutant, differs from its wild-type RSV strain A2 in the fusion (F) glycoprotein and has increased

G when passaged in VERO cell culture (Abstract and page 420, 2<sup>nd</sup> column). Firestone compares F content in the live attenuated RSV strain compared to the parent A2 strain (page 421, Table 1). Firestone teaches attenuating RSV and the comparison of wild-type RSV A2 grown in HEp-2 cells, cold-passages *cp*-RSV, and temperature-sensitive *cpts*-248 (Abstract and page 2872, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph). Firestone teaches how the *cpts*-248/404 mutant differs from its wild-type RSV A2/HEK7 parent (Abstract). Firestone also teaches the predominant nucleotide in *cpts*-248/404 is G and that this can be used for identification of the *cpts*-248/404 mutant (pages 421-422, joining paragraph).

Johnson teaches about RSV glycoprotein (G) and fusion (F) protein and a method of purification of G protein from A2 strain. Johnson teaches vaccination with F protein is more immunogenic than vaccination with G protein. Firestone teaches a live attenuated RSV strain, *cpt*-248/404 mutant, differs from its wild-type RSV strain A2 by increased G and the F gene content.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to identify a high glycoprotein producing RSV. The person of ordinary skill in the art would have been motivated because Johnson teaches the importance of the glycoprotein F and how to measure the glycoprotein, and Firestone teaches a comparison of attenuated RSVs to the wild-type RSV. One reasonably would have expected success because of the teachings of Johnson and Firestone.

#### ***Response to Arguments***

Applicant's arguments filed June 27, 2008 have been fully considered but they are not persuasive. Applicants argue "the references do not teach or suggest a method as claimed for

identifying an attenuated respiratory syncytial virus (RSV) strain that produces high yields of RSV surface glycoprotein F when compared to parent strain A2. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Moreover, Applicants assert that the references do not teach or suggest that the strain so identified by the methods described in the present invention is *cpts-248/404*, which may be grown in eukaryotic cells selected from VERO, MRC-5, FRhL, CEF or PER.C6 cell culture." Firestone teaches RSV is grown in Vero and HEp-2 cells.

Applicants argue "Johnson does not teach or suggest a method of identifying an attenuated respiratory syncytial virus (RSV) strain that produces high yield of RSV surface glycoprotein F, as currently claimed, when compared to parent A2 strain." Johnson teaches a method of measuring and purification of the glycoprotein from RSV A2 strain. Firestone teaches RSV G and fusion (F) glycoproteins are different in the mutant compared to the wild-type A2 (Abstract).

Applicants argue "Firestone does not teach or suggest a method of identifying an attenuated respiratory syncytial virus (RSV) strain that produces high yield of RSV surface glycoprotein F, as currently claimed, when compared to parent A2 strain." Johnson teaches a method of measuring and purification of the glycoprotein from RSV A2 strain. Johnson teaches the G and F proteins are on the surface of RSV. Firestone teaches RSV G and fusion (F) glycoprotein are different in the mutant compared to the wild-type A2.

Applicants argue “There is simply no teaching or suggestion in the references, alone or in combination for **a method of identifying an attenuated respiratory syncytial virus (RSV) strain that produces high yield of RSV surface glycoprotein F**, as currently claimed, when compared to parent A2 strain”. Johnson teaches a method of measuring and purification of the glycoprotein from RSV A2 strain. Johnson teaches the G and F proteins are on the surface of RSV. Firestone teaches a comparison of the G and F proteins in the A2 strain compared to the mutant strain. Applicants argue “that there is no motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings found in the cited references to achieve Applicants’ claimed invention.” Johnson teaches the F protein is more immunogenic than the G protein and they are surface glycoproteins. Johnson is comparing the vaccines prepared with the G and F glycoproteins. It would be obvious to measure the glycoprotein content in the wild-type strain compared to the mutant strain for vaccine production since Johnson teaches the glycoproteins stimulate Th CD4+ production.

Applicants argue “the references cited by the Examiner would not have suggested to one of skill in the art that a *cpts*-248/404 mutant, which replicates poorly in cells at 37°C, could produce a five fold increase in the F glycoprotein at 30°C, thus making it highly desirable candidate for vaccine production.” In response to applicant’s argument that the references fail to show certain features of applicant’s invention, it is noted that the features upon which applicant relies (i.e., produce a five fold increase in the F glycoprotein at 30°C) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON HURT whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

November 4, 2008

/Bruce Campell/  
Supervisory Patent Examiner, Art Unit 1648